In conclusion, we have identified a subset of human dermal APC with protracted survival after HSCT and potential importance in promoting donor T cell reactivity to host antigens.

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LOW DOSE ANTI-THYMOCYTE GLOBULIN FOR GRAFT-VERSUS-HOST DISEASE PROPHYLAXIS OF MISMATCHED UNRELATED PERIPHERAL BLOOD STEM CELL TRANSPLANTATION IN ADULT PATIENTS WITH ACUTE MYELOGENOUS LEUKEMIA

Kim, H.-J., Min, W.-S., Eom, K.-S., Cho, B.-S., Min, C.-K., Lee, S., Cho, S.-G., Lee, J.-W., Kim, C.-C. Catholic HSCT Center, St. Mary's Hospital Catholic University of Korea College of Medicine, Seoul, Republic of Korea.

Anti-thymocyte globulin (ATG) has been introduced in preventing acute graft-versus-host disease (AGvHD) in several studies. Many of them suggest that ATG at a total dose range of 4.5∼15 mg/kg reduces the risk of severe AGvHD but increases the risk of infections. We tried to investigate the role of ATG in HLA-mismatched unrelated hematopoietic stem cell transplantations (uHSCT), specifically in patients who received G-CSF mobilized peripheral blood stem cells (PBSCs) or from allele(s)/antigen mismatched unrelated donors from worldwide donor registries. Sixty five patients with intermediate to unfavourable risk AML who received HLA-mismatched uHSCT from the available Asian as well as Caucasian donors were enrolled. We compared 2 different groups according to the use of ATG (group 1) or not (group 2). The addition of ATG (thymoglobulin, Genzyme), at a dose of 1.25 mg per kilogram of body weight per day for 2 consecutive days, for recipients who received either PBSCs and/or from mismatched unrelated donors (group 1, N = 35); this was added to prevent the development of AGvHD together with our standard regimen which consisted of methotrexate (10 mg/m^2 intravenously bolus on day +1; and methotrexate 5 mg/m^2 intravenously bolus, on days +3, +6, +11) and tacrolimus starting at day –1. G-CSF was administered in all patients at a dose of 5 mg/kg subcutaneously per day from D + 7 after transplantation until neutrophil recovery. The median age was 38 (range, 16–65) and the median follow-up duration was 24 months (range, 3–72). The majority of patients had intermediate or unfavourable cytogenetic features. The main conditioning regimen consisted in cyclophosphamide plus total body irradiation. The transplanted patients were all successfully engrafted. The median time to neutrophil (>0.5 × 10^9/kg) and platelet (>20 × 10^9/kg) recovery was 15 vs 17 days, 14 vs 17 days in the group 1 and 2, respectively. The overall incidence of AGvHD and chronic GvHD was 38% and 41%; 33% and 35%, 37% and 48% for patients with group 1 and group2, respectively. Nine (14%) patients were relapsed so far. The comparison of estimated probability of disease-free survival rate at 2-year for each group was 89% vs 74%, respectively. The estimated probability of event-free survival rate at 2-year was 65% vs 51%, respectively. The overall 2-year non-relapse TRM was 14%. These results suggest that the uHSCT performed with a very low dose of ATG (total 2.5 mg/kg) are feasible with a promising outcome.

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TACROLIMUS, SIROLIMUS AND ANTITHYMOCYTE GLOBULIN (rATG) FOR GRAFT VERSUS HOST DISEASE PROPHYLAXIS FOR UNRELATED DONOR HEMATOPOIETIC CELL TRANSPLANTATION

Aljitawi, O.S., Nakamura, R., Palmer, J., Senitzer, D., Pullarkat, V., Briggs, A., Cai, J.-L., Rosenthal, J., Schriber, J., Snyder, D., Nademanee, A., Parker, P., Forman, S. City of Hope Comprehensive Cancer Center, Duarte, CA.

The effect of adding ATG to Tacrolimus/Sirolimus combination in graft-versus-host disease (GVHD) prophylaxis is largely unknown. We reviewed our records for patients who underwent unrelated transplants and received this combination for GVHD prophylaxis. Nineteen patients were identified who received their transplants between 8/06 and 02/07. Median age at time of transplant was 51.1 years (17–61.5). Nine recipients were males and 10 were females. The indications for transplant were as follows: ALL n = 9, AML n = 5, NHL n = 2, MDS n = 2 and CML n = 1. Twelve patients were in remission (CR1 = 10, ≥CR2: n = 2), and seven had refractory disease. Eight patients received reduced-intensity conditioning (fludarbine/melphalan: n = 8) and 11 received full-intensity conditioning (FTBI/VP-16: n = 8, FTBI/Cytoxan: n = 3). All received peripheral blood hematopoietic stem cell products except for two patients who received bone marrow products with the median CD34+cell dose of 6.82 (1.56–9.46) x10^6/Kg. Donors were molecularly matched in A, B, C, and DR in 11 patients; the remaining donors were mismatch in class I (n = 5) or both class I and II (n = 3). After a median follow-up of 9 months 16 patients are alive. Two deaths were related to infections within the first hundred days and not associated with acute GVHD. One patient died of relapsed AML. The probabilities of one-year overall survival, disease-free survival, relapse, and non-relapse mortality were 78%, 80%, 11%, and 11%, respectively. Ten patients developed acute GVHD with median onset of 24 days (7–35 days) after transplantation including five (26%) grade II and two (11%) grade III. We observed no grade IV GVHD in this cohort. Two patients developed chronic GVHD (limited: n = 1, extensive: n = 1). Patients tolerated rATG treatment well except for one who developed atrial fibrillation. Three patients developed thrombotic microangiopathy that required discontinuation of tacrolimus and sirolimus. Six of 15 CMV seropositive recipients developed reactivation of CMV including one with CMV pneumonia. None had reactivation of EBV. Eight patients had at least one documented bacterial infection.

Conclusion: In conclusion, the combination of Tacrolimus/sirolimus/rATG appears to be well tolerated, with a low rate of acute GVHD in this high risk group of patients without increased risk of early relapse or CMV/EBV reactivation. A prospective trial of this new combination in unrelated donor transplants is underway at our institution.

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INTRA-ARTERIAL CATHETER DIRECTED IMMUNOSUPPRESSIVE THERAPY FOR STEROID RESISTANT OR DEPENDENT GRAFT VS. HOST DISEASE (GVHD)

Shapira, M.Y.[1], Bloom, A.I.[2], Or, R.[1], Resnick, I.B.[1], Aker, M.[1], Bitan, M.[1], Slavin, S.[1], Verstandig, A.[2]. [1] Hadassah – Hebrew University Medical Center, Jerusalem, Israel; [2] Hadassah – Hebrew University Medical Center, Jerusalem, Israel.

Introduction: Prolonged treatment of graft vs. host disease (GVHD) is extremely immunosuppressive. Local therapy with intra-arterial (IA) injection of steroids may induce remission with lower extent of systemic immune suppression. Here, we present our experience with IA treatment of gastrointestinal (GI) and/or hepatic steroid resistant/dependent GVHD with 2 consecutive protocols. **Methods:** Thirty five patients (37 GVHD events (hepatic, n = 15), (GI, n = 16), (combined, n = 6)) were treated with 53 IA sessions. **Results:** We found that IA steroid therapy was associated with partial and complete remission among patients with steroid resistant/dependent hepatic or GI GVHD. Hepatic partial response was observed in 14 (66.6%) patients among whom 7 (33.3%) reached complete response. GI partial response was observed in 19 (86.4%) patients among whom 12 (54.4%) reached complete response. Most side effects were minor. An early administration of the local therapy, female gender, myeloid basic disease, and a non-active status of the basic disease at the day of transplantation were found related for predicting a better response for the intra-arterial treatment. The use of high dose steroids in the hepatic IA protocol from was at least as good as intermediate dose steroids with methotrexate and may be safer. **Conclusion:** Intra-arterial catheter guided steroid therapy is safe and effective in steroid resistant/dependent GVHD. Hepatic artery treatment with methotrexate can be safely substituted with high dose IA methylprednisolone. Further research is warranted characterizing the patients benefit most.